## Remarks

Claims 1 through 41 remain pending in the application.

The Office Action maintains the rejections stated in the Office action of September 4, 2007. However, that rejection was based on an assertion that a stent "can be placed in the endocardial or peri-adventitial area, which would mean the therapeutic agent will be injected into the myocardium from these areas." The Office Action maintains and reiterates this rejection, despite the clear inadvisability of placing a stent outside the arteries to treat a stenotic lesion inside the artery. The fact that the claims are found unpatentable based on the assumption that one in the art would install a coronary stent outside the coronary artery is a clear sign that the claims are non-obvious, because the reason suggested for doing so is so blatantly dangerous and deadly to the patient and will not lead to any alleviation of the stenosis of the coronary artery treated with a stent placed in the endocardial or periadventitial space.

Furthermore, at this late stage in the examination, no motivation for making the combination has been proposed. The Office Actions merely state that the elements of the claims can be found dispersed in the art. There has been no indication in the prior office actions of a motivation to make the combination suggested by the Examiner.

The arguments traversing the rejections stated in the Applicant's prior response are reiterated. In addition, Applicant points out that though Stevens mentions therapeutic agents, he does not mention an anti-stenosis agent as suggested

in support of the rejection of claim 1 through 6, 11 through 16, 21 through 26 and 31 through 36. Barry suggests injecting heparin into the blood vessel lumen, but there is no indication that heparin would be beneficial if injected into the myocardium.

Neither the pathway nor the agents usefully employed through the pathway are obvious in view of the cited references. Altman, et al., Exploring Heart Lymphatics in Local Drug Delivery, 1 Lymphatic Research And Biology 47, (2003) illustrates the advantage of the claimed method, which could not have been understood by review of the cited art. The article illustrates the behavior of compositions described in the earlier filed specification of the current patent application. As described in this peer-reviewed article, microspheres injected in the myocardium tend to migrate through the lymphatic system of the heart upstream relative the coronary artery and collect in peri-adventitial heart tissue around the coronary artery. They do not quickly dissipate away from the site. The size of the particles effects the rate at which they migrate, degrade, and release agents that then into the coronary vessel wall. As discussed in the article, particles of 15000 nm (described as 15 um in the specification) remain localized near the site of injection. These larger particles gradually decay and migrate up the outside the coronary artery and slowly release agents to the coronary artery wall. This enables long term release of anti-restenosis agents which otherwise would be quickly washed out of the coronary system will little or no local effect. Thus, the Applicant has discovered a drug delivery pathway that was unappreciated in the art, and has beneficial attributes unappreciated in the art. Accordingly,

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the claims directed to combining use of those pathways with stent placement would not have been obvious. The claims directed toward use of those pathways with stent placement and particular formulations (claims 7 through 9, 17 through 19, 27 through 29 and 37 through 39, and claims 10, 20, 30 and 40) would not have been obvious, for the additional reason that the cited art does not suggest any particular motivation to use those formulations in combination with stent placement or periadventitial delivery.

## Conclusion

This response has addressed all of the Examiner's grounds for rejection. The rejections based on prior art have been traversed. Reconsideration of the rejections and allowance of the claims is requested.

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